Rachel: So, this is Douglas Densmore. PI in the lab, from our records. Alright. Could you please define the term “synthetic biology” and what it means to you?

Doug: I would say that synthetic biology is...I’ve always defined it as the forward engineering of living systems. So as opposed to taking a look at living systems and trying to understand how they work, we try to use what we do understand and use that knowledge to make new living systems. Synthetic biology to me is using knowledge for engineering systems, particularly biological ones and really using engineering principles of abstraction, modularity, and standardization.

Rachel: Awesome.

Marisa: Could you please describe your field of work?

Doug: So my background, my PhD is in electrical engineering and so what I always have done is taken a look at individual components that have rules for how they’re hooked together. When you hook them together with those rules they make more complicated systems. So in electrical engineering, that’s a transistor. We take transistors, we know how they work, and we hook them together to make microprocessors, and cell phones, and things. But we don’t do that with pencil and paper, we do that with computers. My research focuses on how to take the basic building blocks of biological systems, DNA, in this case DNA parts, and how to use software to hook them together using the same principles we would have with electrical engineering. So standardization, hierarchy, composition rules, constraints, performance modeling specifications, things like that. So, I make software for synthetic biology.

Rachel: So why are you performing research in this field?

Doug: That’s a good question. I’m performing research in this field because traditional computer design electronics has kind of plateaued. There are interesting things we can do. I’ll get my Samsung S8 phone or S9, I’ll get a better cell phone, I’ll get a faster computer, and those are important. There are medical applications. There are are safety, critical applications. There are avionics, automotives, smart cars, there are things going on in electronics, in electrical engineering, but I’m in this field because I think I can have more of an impact in synthetic biology. The field is younger. It’s I think...I won’t say faster moving but I think there are more fundamental discoveries happening every day. So, I’m in this field because I like to solve puzzles and I think how we put together biological systems is an interesting puzzle. So, when I got into this field when I had to do a post-doc, so I said well...actually, when I think my PhD, my girlfriend at the time, now my wife, wasn’t finished with her PhD at the time at U.C. Berkeley, we were both at Berkeley, and so I said I can either leave her and go get a faculty job--not leave her like leave her forever, but leave her temporarily and will be apart--or I can stay at Berkeley and do a post-doc. So I said, “What do I want to do differently than electrical?” and so I started learning about biological systems and gates, genetic gates, logic gates, ‘cause that’s what we did in electronics and then built on that. So that was my post-doc. So from 2007 to 2010 I was a post-doc and then came here. So I moved kind of...I’m one of the few people who’s PhDs is truly electrical engineering in synthetic biology.

Rachel: Yeah, no kidding.

Doug: Yeah.

Marisa: Why do you think the public should care about synthetic biology?

Doug: Well, I think there's two reasons. The kind of more pro-active, positive reason is that biology can change the world, it can change our therapeutics, it can change materials, it can save on renewable resources and things like that. So, I think it's in a way a green tech, because biology builds itself. It's renewable. So I think it's got tremendous upsides. That's the very positive, proactive. The more pragmatic reason they should care is it's just coming. As we learn more about how to make biology work, people are going to be using it more. No matter what you think about genetic engineering you can't say "Okay we're done. Stop. No one else do anything else" Now that the genie is out of the bottle so to speak. So I think synthetic biology is a platform for us to do it in a systematic engineered approach and so we can get out in front of some of the issues related to ethics, related to safety, just related to our understanding. So, I think synthetic biology, like the public should be interested because not only can it affect their lives, but getting out in front of genetic engineering can be an important thing.

Rachel: So that kind of bleeds into the next question, in terms of synthetic biology and genetic engineering, what do you feel the public is concerned about?

Doug: I think the public is concerned about biology and engineering in general. So I mean we have folks that are worried about engineered food sources, so genetically modified crops and pieces?? because they're concerned about health safety. They're concerned about potential bioterrorism, or are concerned about just accidental release of harmful biological agents into the environment, so I think they're concerned primarily on safety. There's two people: there's safety and ethics. Ethics are kind of a moving landscape. What was ethical in the 1700s probably isn't necessarily ethical now. Our ethics change. I don't think we should have some moral ambiguity but ethics are kind of dynamic. Safety is pretty constant. People don't want to die in the 1700s, people don't want to die in 2016. So safety is something I think we need to attack on a technical level and ethics is something I think we need to do through a dialogue. So I think between those two, so if we engage the public on dialogues about ethics and I were to tell you I can cure your cancer with a biologically engineered organism, people probably would say that's ethically a good thing to do. If I were to say I could make a company a lot more money with this biologically engineered organism, that may not be as ethically acceptable. So that dialogue is one thing and on safety--actually, I think synthetic biology is well positioned to deal with safety because engineering let's us build in safety mechanisms. If I just randomly assembled an airplane, I probably wouldn't have, you know, redundant electronic systems, I wouldn't have safety checks before you take off, etc. etc. etc. So I think biology, and synthetic biology in particular, allows us to put those checks in place, both biologically and from a protocol and procedural standpoint.

Marisa: So, how do you make people interested in your work in synthetic biology?

Rachel: By "people" we mean more non-scientific people.

Doug: Non-scientific. How do I make non-scientific, well, the danger, the difficulty with synthetic biology is this fine line between scientific credibility and hype. So you can get people excited about synthetic biology. I think about by saying what we are going to do in synthetic biolog is were going to terraform Mars. We're going to make Mars inhabitable. We're going to make pills you can't take that read your genetic information and give you diagnoses about future states, like if "Are you susceptible to cancer?", "Are you going to get Alzheimer's?" So I think the public

can get excited about these science-fictiony kind of stories, which who knows! Maybe we'll get there. But then balancing with the more pragmatic, like "Oh, I discovered a new promoter today." Then they're like "What? I'm not very excited" and so, mainly we get the public by talking about success stories today. So when we talk about the things like the folks at Jay Keasling and his group have done at Berkeley with making antimalarial drugs, so talk about drugs that we can make today with synthetic biology. We can talk about biofuels, we can talk about materials, flavors and fragrances. So I think we can get people to talk about tangible things today, I mean people are interested in--my wife gardens, and you know I think she would love to have you know you can design designer flowers that are different colors or you can have your garden all color coordinated. I think there are some interesting things you can talk about today that get people excited. I think that the bigger thing that people associate with biology in popular media. There's not many movies about biology being good. If you look at movies, biology is like *The Walking Dead* or it's like biology...something happening from a scientific community that hurts the public. We don't talk about--we don't have movies where things like *Lorenzo's Oil* or things where we talk about biological discoveries helping people and so I think getting more of those out into the public. Like how do people know that polio is--that vaccine was a biological process, medicines are biological processes, but they don't associate that with engineering for somehow. Like people are just in the lab and they figured it out and made a solution. They don't think about all the engineering and science that went into that. Educating them.

Rachel: Kind of hopping off of what you said about polio real fast--

Doug: Umm hmm.

Rachel: A lot of people don't realize that polio was actually, the polio vaccine was actually created using HIV. Do you think that the vectors that we use in synthetic biology that we use to make these astounding cures would change the public's opinion on these cures?

Doug: Yeah, perhaps. I think more education in general. It's always hard to say 'cause some of these words are so polarizing like…

Rachel: HIV vaccine?

Doug: Yeah. Exactly. And as soon as you say...and I still--you guys in some ways have a lot more biological knowledge than I do. I'm still ignorant on lots of things. So, when I got into synthetic biology, I hadn't had a biology class since ninth grade and bacteria are bad 'cause when you watch a TV show, I mean a commercial, everything is killing bacteria. This kills bacteria. This kills bacteria. Bacteria are bad and viruses sound even worse, so it's really hard to get people into the subtleties. You interview people and they're like, "I don't want DNA in my food." So they don't basically understand what DNA is. So it's really hard. I think we just really have to keep getting some success stories and somehow people are positive and relate back to those success stories. The polio vaccine, maybe we don't start with saying, "Oh you know pieces of the HIV virus were used in that." That might be a little crazy. But just say we have those vaccines. But it's hard. In some ways we've made negative progress. We might have people who are anti-vaccine. Vaccines might seem like a positive thing, but it's a difficult challenge. And I think it will be increasingly--come to the forefront as we need these more and more. So right now I think America feels we can eat pretty well without genetically engineered

organisms, but I don't think they haven't thought of the global view on how people can eat across the world.

Rachel: What kind of interactions do you have with the non-scientific community?

Doug: The interactions I have with the non-scientific community are relatively limited. Most of my day is with scientific folks. I have opportunities to interact with people through specific talks, when I give open talks to the public. Sometimes I will give people interviews in journals and magazines, sometimes make it out to the general public. I'm not really the best spokes person, I think for synthetic biology. I wouldn't advocate for me to be there and I think that's because of my biology background, that I'm not the best spokesperson. I think I'm a good spokesperson for computing in biology, but that's already, that's a little abstract. I think people like the idea, but I think I can advocate that we can use computing technology to change biology. That's empowering to people because people know how to use a computer. Everyone today, I would make a case that everyone between the ages of six and thirty for sure, probably even more than that, but everyone has used a computer in that range. Probably even to like forty-five or something. So everyone has used a computer, not everyone has used a pipette. Not everyone has gone into a wet lab. But everyone can be like "Oh, the same way I typed on my computer and could write, could make a website, I could also, you know, make synthetic nylon with bacteria. That'd be pretty cool. Or some material. The biggest way I can outreach I think with people is to get them excited about if you use computers what you can do. I'm probably not the best person to interact with people about what you can do with biology just because my background runs out quicker than a PhD level biologist. But again, the main way I interact with people is through conferences. I don't talk to the public very frequently.

Marisa: How would you say would be the best way to get the correct scientific knowledge out to the public, do you think? Do you think it's going to these conferences and then having certain people from these conferences that understand that, go to the media and express it? What do you think is the best trail or pathway to the public, if that makes sense?

Doug: Yeah. No, the best way to the public--there are lots of folks that are explicitly involved in public policy. I don't know who you guys are interviewing, but there are some folks, there is a guy, Ken Oye at MIT, for example, he's one of the very visible public policy voices in synthetic biology. I think those people are well...they don't have the biology background but they do understand how to interact with the public. I think the best way is for you to take your science, distill it down into like maybe the two or three main points, and then work with somebody in policy to figure out how to convey that. And I would convey that typically to younger people, to get them excited, get them thinking about, "Oh, I could do this when I get to high school, or I get to college." So whatever level you're working with, when I get to grad school or whatever. I think that is the best way. It's kind of this tricky. Engagement with the public can be a tricky thing. So you guys may have heard of this glowing plant, have you heard of the glowing plant?

Racel: Which one?

Doug: So there's a Kickstarter project run by this group that did a glowing plant and their goal was to raise all this money, and if you helped them they gave *Arabidopsis* seeds that could glow as part of the kickstarter. It was kind of a big deal because not only did they raise hundreds of thousands of dollars, but it changed, it made Kickstarter think about their model. Kickstarter is typically for artists, like you're making a film or you're making a painting, or doing something, or

you're doing some project but it's not really for science fundraising and so it made Kickstarter rethink their model and made people think about, well, they raised all this money. It's like they're making a glowing plant or is there regulation? So in some ways the glowing plant was a positive thing because it made people reevaluate all this. On the other hand it also played to some of people's biggest fears. People are giving out seeds. And they were well intentioned I think. I think they're goal was not to scare people. So the point is if you were like what we're going to do as an iGEM team is we're going to go out on the corner here of COM and have a little booth and say come learn about synthetic biology. That's particularly, that could be very risky, because depending on--let's say you're tired at the end of the day or have an off day and say something to someone and then write it up something "B.U. students making crazy stuff in the lab" and then suddenly that drowns out all the good you did. So it's kind of damned if you do, damned if you don't sometimes with the public. And so sometimes I think that's why scientists shy away from that because we need to engage in the public but that messaging is so difficult 'cause we're building--it's not like I'm trying to explain what DNA is. That would be tough enough. Now to say we can take DNA and manipulate it. As soon as you say "manipulate" or "change"-- that's not the right word, maybe I need to use something else. There's a whole part to it. I don't know if I answered your question. Good luck transcribing all of this!

Rachel: So, judging off of what you just said, do you think that, maybe not you necessarily adequately reach out and inform the non-scientific community about work or just in general, the field. Do people adequately talk to the non-scientific community or do you think there could be more communication?

Doug: I think there could be more communication. And I think synthetic biology is--it's a group effort. So here at BU, right, we're building this Biological Design Center, it's going to be in this new building and as that kicks off, part of that effort is going to be the messaging around that. That's why we hired Jessica Titel, the executive director of that to help me and Mo and Wilson and Chris. We'll probably have additional PR people at BU. It's a process. We talk about the science, those people massage that into a message. We need this team effort to get this message out. I don't think it's one person's responsibility and I think very few people can do it well. Like if you recall, George Church at Harvard, I remember when I first got here, he was talking about resurrecting woolly mammoths, he's interested in things like that, reviving extinct species. And he's also interested in--he had talked earlier about a Neanderthal. And I remember part of that, because he was talking to the Huffington post online about if we could bring Neanderthals back and to me that's such a crazy, far away goal. Like we're trying to get *E. coli* to glow in response to things. But again, he's somebody who makes big statements because that's kind of what he's interested in doing. He's getting people thinking about new ideas.

Rachel: Is your research publicly funded through the NSF, NIH, etc., or funded privately by non- or for-profits?

Doug: It's both. So it's funded primarily by NSF and DARPA. So it's funded by those two organizations primarily but I do have some funding from corporations.

Marisa: Would you say that you're adequately funded in order to do your research?

Doug: Yes, I have. I am adequately funded. I've fortunate to get the grants that I've applied for.

Rachel: I heard recently that you got a ten million dollar grant or something like that.

Marisa: From the NSF.

Doug: We did. There's an NSF Expeditions in Computing Award and it's through the CISE director. The C-I-S-E, Computer Information Systems Engineering directorate. It's the computer science part of NSF. And so most of these awards are for people thinking about interfacing with computing, low power computing, new computing paradigms, like with electronics. So overwhelmingly their awards are to computer scientists. There are two projects that are unique because they are for biology. One is the Molecular Programming Project led by Erik Winfree at Caltech and that looks at DNA computing, like strand displacement computing. So you have DNA strands and if you leave toll roads exposed, single stranded parts of the DNA, you can have additional DNA that is homologous to that binds, then displaces a strand that goes connects to another one and you keep this chain reaction. So he's interested in how to use DNA to compute like that. DNA origami for actual physical structures. So that's one part, the Molecular Programming Project. We were the second project, we're the Living Computing Project and that is the thing about, if we were two bacterium, we're communicating. How fast is that? If we were to do it on a computer, we would say we are on gigabit ethernet. We know how fast we're communicating. Or if we're on a cell phone, we know what network we're on. Or if I'm on a processor, how many megahertz. But we don't have these metrics for biology. If I want to convey biological information, well what's the rate? What's the power consumption? Is it digital to analog? So that project was five years, ten million dollars, to come up with those principles. So I am well funded in that way and I have another thing, the MIT Broad Foundry through DARPA. So at the Broad Institute at MIT, they've joined together to make this kind of design, large-scale, industrial pipeline for design where we can design, use interesting design approaches to make synthetic biological systems. And so my software powers a lot of that effort as well. But the biggest challenge I have is finding programmers and people from computing who want to do biology. I know a lot of biologists that want to do biology, but it's harder to find computer folks. You can go to Google and make $150,000 a year right out of undergrad or you can come work for me as a grad student and not make $150,000 a year. So it's hard to keep undergrads and the same with grad students. There's a lot of money in computing.

Rachel: That makes sense.

Marisa: Do you feel like your research is protected from infringement?

Doug: No. I'm really--So the way that this would work in academia is that your currency is publication. So if you publish something, then it's presumably public. Someone could take my ideas and make them. What you're supposed to do, is work with your university and file what's called a provisional patent before you do this because there's no way you can wait for your full patent to be issued before you publish because full patents can take a couple years. Provisional patents are relatively quick, they're a placeholder while the patent is in process if you file this provisional it gives full protection while this patent is in process. BU is well intentioned and i don't know where this interview is going to go. BU is well intentioned but they simply don't have, right now, the bandwidth to handle all of the provisional patents that I, Wilson, Mo, anyone would be equipped to put out. I mean I publish at a computer science rate, probably a paper every six months, if not more, and so I would be putting out...It'd be difficult. So the short answer is no I don't feel adequately protected but the nice thing is that in my academic life I

don't care that much because my point is that I like change in society. I have a start-up though, and that startup company, Lattice Automation, that is more interest in trying to protect things. So then we have to work explicit with a law firm to protect certain things. But a big part of synthetic biology early on has been this kind of quote-on-quote "hippie" socialist mentality where we should be sharing. That it's not my idea to find some specific parts and keep them. iGEM is indicative about that, right? You make your parts, you share them. It's not like all my special parts that i've patented and no one can use them. I think that's healthy.

Rachel: So, I'm guessing you have a strong opinion of the CRISPR/Cas9 ownership case that's going on between MIT, UC Berkeley, and what was the other one? Harvard? Caltech? I always forget which one.

Doug: It's Harvard. Yeah, they're still--UC Berkeley, MIT, Harvard, it depends on how you count things...it's funny...I actually don't have as strong of an opinion as you might think on it. I don't actually know enough about the finite details to say who I think is right or wrong. I think what it's largely...I'm trying to think of what i think it's indicative of...Well now there's a lot of cooks in the kitchen.

Rachel and Marisa: Yeah

Doug: So now there's a lot of cooks. There's a lot of lawyers, people smell money and so when people smell money, it goes on. It's going to get more and more ambiguous. I think technology is sort of--I would hope they could separate the technology from proprietary advances, If I were to patent, like the wheel...it's a pretty good patent but it would limit the ability for us to do a lot of things. Though I think of the wheel as a tool. I think automakers have lots of patents, none of them involve just "the wheel" and they're somehow successful. So I would hope that therapeutic manufacturers, other people can patent certain things that give them competitive advantages without patenting the CRISPR, some of the particular technology. I think patenting technology can be difficult because then it prevents other people from doing--if it's really that powerful it seems like it could be a thing that can be shared with a lot of folks. And I'm sensitive to certain patents where a lot of money has gone into that. And I'm not saying that that hasn't happened with CRISPR but, I don't know if it's been a billion dollars worth investment on the inventors side. I think just practically speaking that couldn't have been possible. So, it's not like I went off, spent a billion dollars of my own money, came up with something and now I need to recoup that cost, this largely academic research that academic industries, or institutions want to claim credit for. But again, I don't know a ton about it.

Rachel: That makes sense. Ok. Going back off of your research being protected from infringement, and you feeling like it isn't, but that it doesn't matter, does this fear or this feeling that you're not being protected, impact your openness to discuss your work with anyone? like the public?

Doug: No. I'm actually, because I'm in a field most of what I do is I make ideas and then I turn those ideas into software. And so I feel like ideas are cheap. Like, I can come up with ten new ideas a day and then code them up and they're different and new. I'm really open. I'm like strangely open to my biologist colleges. I mean you guys work on something for weeks, months, years and it finally works and then you're like "ahh!"

Rachel: So true.

Doug: Whereas, we work for years on software, but if I work for an hour a day, I will have working code, of some sort. If you work for an hour a day, maybe nothing worked, maybe you threw it all away--

Rachel: I'd probably do a miniprep or something.

Doug: Yeah. You just throw it all away. So, it's a different thing. It's not all of software, but I'm in academia because i just want to--my salary isn't dependent on this. Like, I'll get paid if I have a patent. I get paid if I don't have a patent. What I want to do is...it's kind of like I'm a brand, like my group needs to be a brand because I need to track their tab, I need to check grants, and how a brand gets out there, if it was all based on patents then it would take a long time for me to get my brand out there. So you need to talk about things early, often, frequently. And if every time I gave a talk and said "Well, this is protected. This isn't..." And I actually love the people that copy me. I wrote an algorithm on how to put DNA together and somebody took that and beat it. Didn't beat it in terms of the quality, but they beat it in terms of the speed and I thought that was pretty cool. So I said, "That's good." Somebody actually took something that I wrote, a paper that I wrote in 2010. They tweaked it and made it better. And that was good.

Rachel: That's really cool.

Doug: If I was hurting my ability to do work, that might be one thing but I'll just come up with another idea.

Rachel: Alright, this is our last question.

Doug: Yeah.

Marisa: What regulations do you feel should be placed on synthetic biology?

Doug: I think the same regulations that are placed on molecular biology. That's kind of a cop out. But if I'm doing BSL level, you have all your biosafety level protocols, I think none of that needs to change for synthetic biology. I think the same things that we do for BSL1, BSL2, etc. those are sufficient for biology, synthetic biology. I think most of these are covered by the recombinant DNA safety protocol procedures we have. I don't think there needs to be anything specific for synthetic biology.

Rachel: So do you feel any of these regulations should be lifted or is it all just the same?

Doug: Yeah, I currently feel pretty good with the regulation landscape in my research, admittedly. I'm basically prokaryotic *E. coli* trying to move to cell free. So I'm somebody who's on one end of the spectrum. You might talk to someone who's done a lot of mammalian work, talk to like James Galagan who works at The Needle who worked with tuberculosis. Those folks might have stronger feelings. James might be a good person to interview. If you guys don't have James Galagan on your schedule, you should interview him.

Rachel: We were aiming at these PIs first.

Doug: Okay, okay. But once you get those PIs, talk to James, he's easy to talk to. And you know he also works at the Needle. But my general feeling on...I think the regulation is sufficient, but I don't have anything to hide so I would encourage, like, I think the public should continue to be involved to the extent that the public wants to have a real dialogue. Sometimes the public, like if the public dialogue is like "No synthetic biology!" then it's hard to have a dialogue, right? If they come into the meeting protesting saying "No synthetic biology! Cancel it!" then how do we start the discussion?

Rachel: I lied. I do have one more question.

Doug: That's fine.
Rachel: This is the last one.
Doug: That's fine.
Rachel: How comfortable are you with public policies and regulations surrounding your field? Do you feel you are well versed in all of the regulations you need to know or do you feel kind of shaky?
Doug: I'm not well versed. So what I do...I'm versed in what I need to do for BU. That's material transfer agreements, that's safety protocols relating toward the health and human safety kind of requirements here. So I'm here...whenever I make DNA, get DNA out with the material transfer agreements, we send DNA to AddGene and other places. I'm familiar with those regulations. I'm familiar with the training like folks like you have to go through in the lab and I'm familiar with policies in terms of disclosures of export control, like where we're sending this thing and in terms of where my publications are available.
Rachel: Alright. I lied again. I have one more question. It's just one more this time.
Doug: Alright, I'll try to keep it short then in case you have any more questions.
Rachel: No. I'm sorry. I don't want to take up too much of your time than we've already got.
Doug: That's fine.
Rachel: So, my question is would you find it useful to have a review article or a small pamphlet that outlines major regulations that are relevant to you in your field or do you feel like you know what you need to know well enough that you wouldn't find that useful at all?
Doug: I guess the answer to that is, to make it yes or no, is yes.
Rachel: You would find it useful?
Doug: Yes.
Rachel: Do you think you would use it semi-often or do you think it would just sit in your desk and be all, like "Yeah, that thing exists."
Doug: I would read it and then I would make a note of what we're adhering to, the things that we're not adhering to, I would end up delegating.
Rachel: That makes sense.
Doug: So the short answer...what we need to be inventing is a time machine, because that's what I need more of is time. So everything that I do takes up some or one of the twenty-four hours in a day. The safety pieces obviously are a priority, so I would make sure we're adhering to them. When it comes to a lot of reporting, additional mechanisms, that becomes another thing that I have to do and so its probably not the best use of my time, because I'm not in the lab doing science, but for someone like a tech, like Mary.
Rachel: That makes sense. Alright. Cool.
Doug: I'm not the best person to do anything. So you'll find like professors, like we're good at raising money, at generating ideas, and at steering the ship, but not like in the engine room. You don't want professors in the engine room monkeying around. Very few, because they got to go back and steer the ship. If they're in the engine room, they're not steering the ship. They haven't been the headman in the engine room for ten years and they're like "What's this lever do?" and they're like "No, I just tuned that lever! Don't do that!" Or they're really slow at shovelling coal in the engine, or whatever. So, most of my work is best served where I can make the biggest impact. And that's mainly making sure the lab follow procedures.

Rachel: Phenomenal. Alright. Cool.
Marisa: Thank you for your time.
Rachel: That's it.
Doug: That's it?
Rachel: Yeah, thank you!